

AMENDMENTS TO THE CLAIMS

Listing of the Claims:

1. (previously amended): A compound for inhibiting expression of angiogenin comprising an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding human angiogenin.

2. (previously amended): The compound of claim 1 wherein the base sequence binds to the target portion of the nucleic acid in a manner to inhibit the expression of angiogenin.

3. (previously amended): The compound of claim 2 wherein the oligonucleotide analog comprises a modification selected from the group consisting of a modified internucleotide linkage, a modified purine or pyrimidine moiety, a modified sugar moiety, a modified 5' hydroxyl moiety, a modified 3' hydroxyl moiety and a modified 2' hydroxyl moiety.

4. (previously amended): The compound of claim 3 wherein the modified internucleotide linkage comprises a substituent having an improved aqueous or lipid solubility or improved resistance to nuclease digestion as compared to an unmodified compound.

5. (currently amended): The compound of claim 4 wherein the modified internucleotide linkage is selected from the group consisting of phosphorothioate, N-alkyl phosphoramidates, cycloalkyl phosphoramidates, alkyl phosphonates, cycloalkyl phosphonates, ~~phosphodiester~~, phosphotriester, C₁ - C₄ alkyl, cycloalkyl, short chain heteroatomic backbone, short chain heterocyclic backbone, morpholino backbone, polyprotein-nucleic acid backbone, peptide-nucleic acid backbone, polyamide, CH₂-NH-O-CH₂, CH₂-N(CH₃)-O-CH₂, ~~CH₃-O-N(CH₃)-CH₂~~ CH₂-O-N(CH₃)-CH₂, CH₂-N(CH₃)-N(CH₃)-CH₂, and O-N(CH₃)-CH₂-CH₂.

6. (original) The compound of claim 3 wherein the modified purine or pyrimidine moiety includes inosine.

7. (original) The compound of claim 3 wherein the modified sugar moiety includes sugar mimetics comprising C₄ - C₈ cycloalkyl.

8. (previously amended): The compound of claim 3 wherein the modified 5' or 3' hydroxyl moiety is selected from the group consisting of C₁₋₄ alkoxy, intercalating agent, peptide, enzyme, and ribozyme.

9. (currently amended): The compound of claim 3 wherein the modified 2' hydroxyl moiety is selected from the group consisting of C₁ to C₁₀ lower alkyl, substituted lower alkyl, substituted lower alkaryl substituted lower aralkyl; Cl; Br; CN; CF₃; OCF₃; O, S, N-alkyl; O, S, N-alkenyl; SOCH₃; SO₂CH₃; ONO₂; NO₂; N₃; NH₂; heterocycloalkyl, alkaryl; aminoalkylamino; polyalkylamino; substituted silyl; an RNA cleaving group; a cholesteryl group; a conjugate; a reporter group; an intercalator; and a group for improving the pharmacokinetic properties of an oligonucleotide as compared to an unmodified compound.

10. (original) The compound of claim 1 wherein the base sequence of the oligonucleotide or analog thereof is selected from the group consisting of

5'- GCCCATCACCATCTCTTC - 3',

5'- ACACGGCATCATGAATCA - 3',

5'-CCAGGGGCCCCGCTGGTTA-3',

5'-ACCAAATTTTATATTCTA-3',

5'-CAGGCCCATCACCATCAC-3',

5'-GCCCAGGCCCATCACCAT-3', and

5'-TCTCTGACACGGCATCAT-3'.

11. (previously amended) A composition for inhibiting expression of angiogenin comprising an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding human angiogenin in a pharmaceutically acceptable carrier.

12. (original) The composition of claim 11 wherein the base sequence of the oligonucleotide or analog thereof is selected from the group consisting of

5'- GCCCATCACCATCTCTTC - 3',

5'- ACACGGCATCATGAATCA - 3',

5'-CCAGGGGGCCCGCTGGTTA-3',

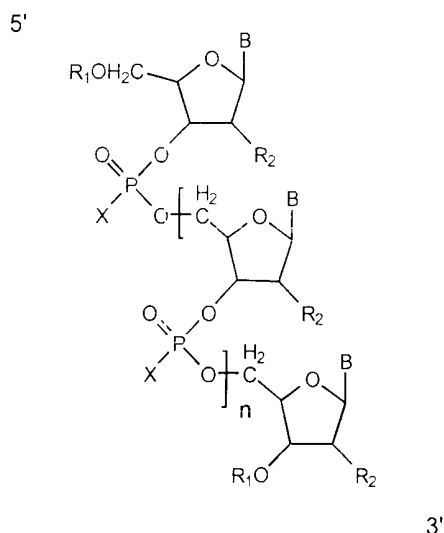
5'-ACCAAATTTTATATTCTA-3',

5'-CAGGCCCATCACCATCAC-3',

5'-GCCCAGGCCCATCACCAT-3', and

5'-TCTCTGACACGGCATCAT-3'.

13. (currently amended): A compound for inhibiting expression of angiogenin having the formula:



wherein

X is selected from the group consisting of O, S, and C₁₋₄ alkyl;

B is selected from the group consisting of adenine, guanine, cytosine, and thymine, selected such that the oligonucleotide has a complementary base sequence with a portion of a target nucleic acid strand coding for human angiogenin thereby inhibiting expression thereof;

R₁ is selected from the group consisting of H, C₁₋₄ alkyl, intercalating agent, peptide, enzyme, and ribozyme;

R₂ is selected from the group consisting of H, OH, SH, SCH₂, OCH₃, F, OCN, OCH₂CH₃, OCH₃OCH₃, OCH₂OCH₃, OCH₃O(CH₂)_pCH₃, OCH₂O(CH₂)_pCH₃, O(CH₂)_pNH₂, O

(CH₂)_pCH₃, where p is from 1 to about 10; C₁ to C₁₀ lower alkyl, substituted lower alkyl, substituted lower alkaryl, substituted lower aralkyl; Cl; Br; CN; CF₃; OCF₃; O, S, N-alkyl; O, S, N-alkenyl; SOCH₃; SO₂CH₃; ONO₂; NO₂; N₃; NH₂; heterocycloalkyl, alkaryl; aminoalkylamino; polyalkylamino; substituted silyl; an RNA cleaving group; a cholesteryl group; a conjugate; a reporter group; an intercalator; a group for improving the pharmacokinetic properties of an oligonucleotide as compared to an unmodified oligonucleotide; and a group for improving the pharmacodynamic properties of an oligonucleotide as compared to an unmodified oligonucleotide; and

n is 5 to 100.

14. (original) The compound of claim 13 wherein the base sequence is selected from the group consisting of

5'-GCCCCATCACCATCTCTTC-3',

5'-ACACGGCATCATGAATCA-3',

5'-CCAGGGGCCCCGCTGGTTA-3',

5'-ACCAAATTTTATATTCTA-3',

5'-CAGGCCCATCACCATCAC-3',

5'-GCCCAGGCCCATCACCAT-3', and

5'-TCTCTGACACGGCATCAT-3'.

Claims 15 – 23 (cancelled)

24. (previously amended): The compound of claim 5 wherein the phosphorothioate is selected from the group consisting of alkyl phosphorothioate, cycloalkyl phosphorothioate, and phosphorodithioates.

25. (previously amended): The compound of claim 8 wherein the intercalating agent is a substituted acridine.

26. (previously amended): The compound of claim 13 wherein the intercalating agent is a substituted acridine.

27. (previously amended): The compound of claim 25 wherein the substituted acridine is selected from the group consisting of 2-methoxy-6-chloro-9-pentylaminoacridine, N-(6-chloro-2-methoxyacridinyl)-O-methoxydiisopropylaminophosphinyl-3-aminopropanol, and N-(6 chloro-2-methoxyacridinyl)-O-methoxydiisopropylaminophosphinyl-5-aminopentanol.

28. (previously amended): The compound of claim 26 wherein the substituted acridine is selected from the group consisting of 2-methoxy-6-chloro-9-pentylaminoacridine, N-(6-chloro-2-methoxyacridinyl)-O-methoxydiisopropylaminophosphinyl-3-aminopropanol, and N-(6 chloro-2-methoxyacridinyl)-O-methoxydiisopropylaminophosphinyl-5-aminopentanol.

29. (currently amended): The compound of claim 3, wherein the modified 2' hydroxyl moiety is selected from the group consisting of OH , SH , SCH_2 , OCH_3 , F , OCN , OCH_2CH_3 , OCH_3CH_3 , OCH_2OCH_3 , $\text{OCH}_3\text{O}(\text{CH}_2)_n\text{CH}_3$, $\text{OCH}_2\text{O}(\text{CH}_2)_n\text{CH}_3$, $\text{O}(\text{CH}_2)_n\text{NH}_2$, $\text{O}(\text{CH}_2)_n\text{CH}_3$, where n is from 1 to about 10.

30. (previously added): The compound of claim 3, wherein the modified 2' hydroxyl moiety is a conjugate.

31. (previously added): The compound of claim 3, wherein the modified 2' hydroxyl moiety is a group for improving the pharmacodynamic properties of an oligonucleotide as compared to an unmodified compound.

32. (previously added): The compound of claim 3, wherein the modified 2' hydroxyl moiety is a group for improving the pharmacokinetic properties of an oligonucleotide as compared to an unmodified compound.